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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,533	09/05/2000	Dominique P. Bridon	C2077-9000	3921

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1648	

NOTIFICATION DATE	DELIVERY MODE
01/31/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/623,533	BRIDON ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6,19,21,31,36,38,39 and 59-98* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6,19,21,31,36,38,39 and 59-98* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/01/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

37 C.F.R. § 1.114

A request for continued examination under 37 C.F.R. § 1.114, including the fee set forth in 37 C.F.R. § 1.17(e), was filed in this application after final rejection on 30 October, 2007. Since this application is eligible for continued examination under 37 C.F.R. § 1.114, and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. § 1.114.

Status of the Claims

Claims 1, 4, 6, 19, 21, 31, 36, 38, 39, and 59-98 are pending in the instant application.

37 C.F.R. § 1.98

The information disclosure statement filed 01 November, 2007, has been placed in the application file and the information referred to therein has been considered.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as

> prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1, 4, 6, 19, 21, 31, 36, 38, 39, and 59-98 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bolognesi *et al.* (1995), hereinafter referred to as the '944 patent, Barney *et al.* (2001)[1], hereinafter referred to as the '782 patent, in view of Sivam *et al.* (1992), hereinafter referred to as the '944 patent, and Narazaki *et al.* (1996). The claims have been amended to specify that the polypeptide portion of the conjugate contains anti-fusogenic acticity. The claims are directed toward anti-HIV peptide albumin conjugates, and compositions comprising said conjugates. The peptides encompassed in the claimed subject matter are SEQ ID NOS.: 1, 3-5, 117-119, and 534-541. These polypeptides correspond to the HIV-1 fusion inhibitor DP-178 (SEQ ID NO.: 1). Amino acid sequences 3-5 are DP-178 analogues, amino acid sequences 117-119 correspond to DP-178 amino-terminal truncations, and sequences 534-541 correspond to DP-178 variants with truncations and conservative amino acid substitutions. The claims further

stipulate that the conjugates a linked via a maleimide-containing group and covalently bind to cysteine 34 (Cys^{34}) in a ratio of 1:1. Additional limitations pertaining to the nature of conjugation were provided in new claims 89-98 (i.e., the linking group is (2-amino) ethoxy acetic acid).

As previously set forth, the '933 patent and the '782 patent both disclose the claimed polypeptides, or obvious variants thereof. The claimed polypeptides, or obvious variants thereof, are all present in the prior art. For instance, SEQ ID NOS.: 1 and 5 are disclosed in the '933 patent (see Figure 13A and SEQ ID NO.: 5) and SEQ ID NOS.: 3, 4, 117-119, and 534-541 (see SEQ ID NOS.: 1357, 1515, 638, 800, 62, 15, and 642) are set forth in the '782 application. These polypeptides are efficient at inhibiting HIV-1 virion-cell fusion. These teachings do not disclose HSA conjugates employing a maleimide linkage at Cys^{34}.

The '944 patent provides conjugates comprising an active component and human serum albumin (HSA). These conjugates are prepared using a maleimide linkage (e.g., see col. 5, lines 13-36; col. 6, lines 46-63; col. 7, lines 34-59) and form a 1:1 ratio of protein:albumin. This teaching notes that protein-albumin conjugates have several favorable properties such as improved half-lives as compared to unconjugated peptides (see col. 1, lines 7-10; col. 3, lines 49-53). This teaching does not disclose HSA conjugates that are linked through Cys^{34}.

Narazaki and colleagues examined the binding interaction between human serum albumin (HSA) and drugs containing thiol groups and determined that this interaction takes place through Cys^{34}.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare conjugates comprising DP-178 and derivatives thereof, as taught by Bolognesi *et al.* (1995) and Barney *et al.* (2001), and

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[1] The '782 patent has an effective filing date of 20 May, 1998.

HSA, as provided by Sivam *et al.* (1992), since Sivam and colleagues teach that protein:HSA conjugates have improved properties such as increased half-lives and greater solubilities. Moreover, one of ordinary skill in the art would have been motivated to utilize Cys^{34}, as identified by Narazaki *et al.* (1996), since this amino acid is located on the surface of the protein and is readily available for conjugation. One of ordinary skill in the art would have also been motivated to use a maleimide linker, or other art-recognized linkers, as disclosed by Sivam *et al.* (1992), since this represents a routine method for preparing thio compounds that readily react with Cys^{34}, as identified by Narazaki and colleagues. Thus, both the motivation and a reasonable expectation of success were present in the prior art.

Response to Arguments

Applicants traverse and submit the claim amendments render the claims nonobvious. It was argued that including the term anti-fusogenic distinguishes over the prior art because there is no suggestion that HSA-conjugates will preserve the antifusogenic activity of the polypeptide. Applicants contend that conjugating DP-178 polypeptides, and derivatives thereof, to a large molecule like HSA would prevent the antiviral polypeptide from obtaining the proper conformation. Reference was made to Shugars *et al.* (1996) suggesting that coupling small antifusogenic peptides to large molecules may result in steric hindrance and reduced antiviral activity. Sivam *et al.* (1992) clearly demonstrate that HSA-protein conjugates have several favorable properties. The fusion proteins of Shugars and associates involved maltose-binding protein (MBP) as a partner. This protein is structurally and functionally different from HSA. The fact that MBP-polypeptide fusions were inactive, does not negate the fact that HSA is a useful carrier for other proteins and polypeptides. There is no data that suggests HSA-

polypeptide conjugates are inactive because of steric considerations. Thus, absent evidence to the contrary, one of ordinary skill in the art would reasonably expect HSA-polypeptide conjugates to have improved pharmacological profiles as compared to the unconjugated polypeptide.

Moreover, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See I*n re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992). However, the prior art clearly provides the requisite peptides of interest and teaches that conjugating said peptides through a maleimide intermediate increases the pharmacological profile of the peptide. Therefore, one of ordinary skill in the art would be sufficiently motivated to combine the references to arrive at the claimed invention. Applicants' representative is invited to contact the Examiner to discuss the rejection further.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered

to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

21 January, 2008